# General

## Guideline Title

Use of psychiatric medications during pregnancy and lactation.

## Bibliographic Source(s)

American College of Obstetricians and Gynecologists (ACOG). Use of psychiatric medications during pregnancy and lactation. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2008 Apr. 20 p. (ACOG practice bulletin; no. 92). [245 references]

## Guideline Status

This is the current release of the guideline.

The American College of Obstetricians and Gynecologists (ACOG) reaffirmed the currency of this guideline in 2012.

# Regulatory Alert

## FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- August 31, 2016 – Opioid pain and cough medicines combined with benzodiazepines : A U.S. Food and Drug Administration (FDA) review has found that the growing combined used of opioid medicines with benzodiazepines or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. FDA is adding Boxed Warnings to the drug labeling of prescription opioid pain and prescription opioid cough medicines and benzodiazepines.
- May 10, 2016 – Olanzapine : The U.S. Food and Drug Administration (FDA) is warning that the antipsychotic medicine olanzapine can cause a rare but serious skin reaction that can progress to affect other parts of the body. FDA is adding a new warning to the drug labels for all olanzapine-containing products that describes this severe condition known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).

# Recommendations

## Major Recommendations

The grades of evidence (I-III) and levels of recommendations (A-C) are defined at the end of "Major Recommendations."

The following recommendations and conclusions are based on good and consistent scientific evidence (Level A):

Lithium exposure in pregnancy may be associated with a small increase in congenital cardiac malformations, with a risk ratio of 1.2 to 7.7.
Valproate exposure in pregnancy is associated with an increased risk of fetal anomalies, including neural tube defects, fetal valproate syndrome, and long term adverse neurocognitive effects. It should be avoided in pregnancy, if possible, especially during the first trimester.
Carbamazepine exposure in pregnancy is associated with fetal carbamazepine syndrome. It should be avoided in pregnancy, if possible, especially during the first trimester.
Maternal benzodiazepine use shortly before delivery is associated with floppy infant syndrome.

The following recommendations and conclusions are based on limited or inconsistent scientific evidence (Level B):

Paroxetine use in pregnant women and women planning pregnancy should be avoided, if possible. Fetal echocardiography should be considered for women who are exposed to paroxetine in early pregnancy.
Prenatal benzodiazepine exposure increased the risk of oral cleft, although the absolute risk increased by 0.01%.
Lamotrigine is a potential maintenance therapy option for pregnant women with bipolar disorder because of its protective effects against bipolar depression, general tolerability, and a growing reproductive safety profile relative to alternative mood stabilizers.
Maternal psychiatric illness, if inadequately treated or untreated, may result in poor compliance with prenatal care, inadequate nutrition, exposure to additional medication or herbal remedies, increased alcohol and tobacco use, deficits in mother–infant bonding, and disruptions within the family environment.

The following recommendations and conclusions are based primarily on consensus and expert opinion (Level C):

Whenever possible, multidisciplinary management involving the patient's obstetrician, mental health clinician, primary health care provider, and pediatrician is recommended to facilitate care.
Use of a single medication at a higher dose is favored over the use of multiple medications for the treatment of psychiatric illness during pregnancy.
The physiologic alterations of pregnancy may affect the absorption, distribution, metabolism, and elimination of lithium, and close monitoring of lithium levels during pregnancy and postpartum is recommended.
For women who breastfeed, measuring serum levels in the neonate is not recommended.
Treatment with all selective serotonin reuptake inhibitors (SSRIs) or selective norepinephrine reuptake inhibitors or both during pregnancy should be individualized.
Fetal assessment with fetal echocardiogram should be considered in pregnant women exposed to lithium in the first trimester.

Definitions:

Grades of Evidence

I Evidence obtained from at least one properly designed randomized controlled trial.

II-1 Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Levels of Recommendations

Level A - Recommendations are based on good and consistent scientific evidence.

Level B - Recommendations are based on limited or inconsistent scientific evidence.

Level C - Recommendations are based primarily on consensus and expert opinion.

## Clinical Algorithm(s)

None provided

# Scope

## Disease/Condition(s)

Psychiatric illnesses during pregnancy and lactation:

- Anxiety disorders
- Major depression
- Bipolar disorder
- Schizophrenia

## Guideline Category

Evaluation

Risk Assessment

Treatment

## Clinical Specialty

Family Practice

Obstetrics and Gynecology

Pediatrics

Psychiatry

## Intended Users

Physicians

## Guideline Objective(s)

- To aid practitioners in making decisions about appropriate obstetric and gynecologic care
- To present current evidence on the risks and benefits of treatment for certain psychiatric illnesses during pregnancy

## Target Population

Pregnant and breastfeeding women with psychiatric illnesses

## Interventions and Practices Considered

- Treatment of depression during pregnancy and lactation*
  - Selective serotonin reuptake inhibitors (SSRIs) (e.g., fluoxetine, sertraline, citalopram and paroxetine)
  - Tricyclic antidepressants (TCAs)
  - Atypical antidepressants (e.g., bupropion, duloxetine, mirtazapine, nefazodone, venlafaxine)
  - Structured psychotherapy such as interpersonal psychotherapy or cognitive behavioral therapy
  - Electroconvulsive therapy
- Treatment of bipolar disorders during pregnancy and lactation*
  - Lithium (including close monitoring of lithium levels)

- Anticonvulsants including valproate, carbamazepine and lamotrigine
- Prenatal surveillance for congenital anomalies by maternal serum alpha-fetoprotein level testing, fetal echocardiography or a detailed ultrasound examination of the fetal anatomy

Treatment of anxiety disorders during pregnancy and lactation*

- Benzodiazepines (alprazolam, chlordiazepoxide, diazepam)

Treatment of schizophrenia during pregnancy and lactation*

- Atypical antipsychotic medications (e.g., clozapine, olanzapine, risperidone)
- Typical antipsychotic medications (e.g., haloperidol, thioridazine, chlorpromazine)

*Note: Psychotropic medications have potentially teratogenic and adverse neonatal effects. The benefits of their use during pregnancy and lactation must be balanced against risks. See the "Major Recommendations" section of this summary and the original guideline document for context.

## Major Outcomes Considered

- Effectiveness of psychiatric medications during pregnancy and lactation
- Teratogenic events, perinatal syndromes or neonatal toxicity related to use of psychiatric medications during pregnancy
- Postnatal deaths

# Methodology

## Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

2008 Original Guideline

The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' (ACOG's) own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985 and June 2007. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document.

Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles.

2012 Reaffirmation

The NCBI database was searched from 2008 to 2012. Committee members conducted a literature search with the assistance from the ACOG Resource Center staff who routinely perform the Practice Bulletin literature searches.

## Number of Source Documents

Not stated

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force.

I Evidence obtained from at least one properly designed randomized controlled trial.

II-1 Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

## Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

## Description of the Methods Used to Analyze the Evidence

Not stated

## Methods Used to Formulate the Recommendations

Expert Consensus

## Description of Methods Used to Formulate the Recommendations

2008 Original Guideline

Analysis of available evidence was given priority in formulating recommendations. When reliable research was not available, expert opinions from obstetrician-gynecologists were used. See also the "Rating Scheme for the Strength of Recommendations" field regarding Grade C recommendations.

2012 Reaffirmation

The Committee on Practice Bulletins - Obstetrics met in October 2012 and reaffirmed this document. A committee member reviewed the document and new literature on the topic. The document was then reviewed by the committee and the committee agreed that it is current and accurate.

## Rating Scheme for the Strength of the Recommendations

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A - Recommendations are based on good and consistent scientific evidence.

Level B - Recommendations are based on limited or inconsistent scientific evidence.

Level C - Recommendations are based primarily on consensus and expert opinion.

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

### Method of Guideline Validation

Internal Peer Review

### Description of Method of Guideline Validation

Practice Bulletins are validated by two internal clinical review panels composed of practicing obstetrician-gynecologists generalists and sub-specialists. The final guidelines are also reviewed and approved by the American College of Obstetricians and Gynecologists (ACOG) Executive Board.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

Appropriate clinical management of psychiatric illness during pregnancy and lactation, which incorporates an appraisal of the clinical consequence of offspring exposure to medications, the potential effect of untreated maternal psychiatric illness, and the available alternative therapies

### Potential Harms

Advising a pregnant or breastfeeding woman to discontinue medication exchanges the fetal or neonatal risks of medication exposure for the risks of untreated maternal illness. Maternal psychiatric illness, if inadequately treated or untreated, may result in poor compliance with prenatal care, inadequate nutrition, exposure to additional medication or herbal remedies, increased alcohol and tobacco use, deficits in mother–infant bonding, and disruptions within the family environment (see Table 1 in the original guideline document). All psychotropic medications studied to date cross the placenta (1), are present in amniotic fluid (2), and can enter human breast milk (3). For known teratogens, knowledge of gestational age is helpful in the decision about drug therapy because the major risk of teratogenesis is during embryogenesis (i.e., during the third through the eighth week of gestation). The U.S. Food and Drug Administration (FDA) has provided a system for categorizing individual medications (see Table 2 of the original guideline document), although this system has considerable limitations. Categories of risk for neonates from drugs used while breastfeeding are also shown in Table 2 of the original guideline.

See the "Major Recommendations" section of this summary and the original guideline document for a detailed discussion of risks associated with psychotropic medication use during pregnancy and lactation.

## Contraindications

### Contraindications

Refer to Table 2 in the original guideline document for a list of psychotropic drugs that are contraindicated in pregnancy and lactation.

# Qualifying Statements

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### Qualifying Statements

These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

# Implementation of the Guideline

## Description of Implementation Strategy

An implementation strategy was not provided.

## Implementation Tools

Foreign Language Translations

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

## IOM Care Need

Staying Healthy

## IOM Domain

Effectiveness

Patient-centeredness

Safety

# Identifying Information and Availability

## Bibliographic Source(s)

American College of Obstetricians and Gynecologists (ACOG). Use of psychiatric medications during pregnancy and lactation. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2008 Apr. 20 p. (ACOG practice bulletin; no. 92). [245 references]

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2008 Apr (reaffirmed 2012)

## Guideline Developer(s)

American College of Obstetricians and Gynecologists - Medical Specialty Society

## Source(s) of Funding

American College of Obstetricians and Gynecologists (ACOG)

## Guideline Committee

American College of Obstetricians and Gynecologists (ACOG) Committee on Practice Bulletins - Obstetrics

## Composition of Group That Authored the Guideline

Not stated

## Financial Disclosures/Conflicts of Interest

Not stated

## Guideline Status

This is the current release of the guideline.

The American College of Obstetricians and Gynecologists (ACOG) reaffirmed the currency of this guideline in 2012.

## Guideline Availability

Electronic copies: None available.

Print copies: Available for purchase from the American College of Obstetricians and Gynecologists (ACOG) Distribution Center, PO Box 933104, Atlanta, GA 31193-3104; telephone, 800-762-2264, ext. 192; e-mail: sales@acog.org. The ACOG Bookstore is available online at the ACOG Web site.

## Availability of Companion Documents

None available

## Patient Resources

The following are available:

- Depression. Atlanta (GA): American College of Obstetricians and Gynecologists (ACOG); 2008. Available from the American College of Obstetricians and Gynecologists (ACOG) Web site. Copies are also available in Spanish.
- Postpartum depression. Atlanta (GA): American College of Obstetricians and Gynecologists (ACOG); 1999. Available from the American College of Obstetricians and Gynecologists (ACOG) Web site.

Print copies: Available for purchase from the American College of Obstetricians and Gynecologists (ACOG) Distribution Center, PO Box 933104, Atlanta, GA 31193-3104; telephone, 800-762-2264, ext. 192; e-mail: sales@acog.org. The ACOG Bookstore is available online at the ACOG Web site .

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## NGC Status

This NGC summary was completed by ECRI Institute on July 21, 2008. The information was verified by the guideline developer on August 11, 2008. This summary was updated by ECRI Institute on May 1, 2009 following the U.S. Food and Drug Administration advisory on antiepileptic drugs. This summary was updated by ECRI Institute on July 20, 2009 following the U.S. Food and Drug Administration advisory on Varenicline and Bupropion. This summary was updated by ECRI Institute on January 8, 2010 following the U.S. Food and Drug Administration advisory on Valproate sodium. This summary was updated by ECRI Institute on March 18, 2010, following the U.S. Food and Drug Administration advisory on Zyprexa (olanzapine). This summary was updated by ECRI Institute on September 15, 2010 following the U.S. Food and Drug Administration advisory on Lamictal (lamotrigine). This summary was updated by ECRI Institute on May 20, 2011 following the U.S. Food and Drug Administration advisory on antipsychotic drugs. This summary was updated by ECRI Institute on September 12, 2011 following the U.S. Food and Drug Administration advisory on Celexa (citalopram hydrobromide). This summary was updated by ECRI Institute on April 16, 2012 following the updated U.S. Food and Drug Administration advisory on Celexa (citalopram hydrobromide). This summary was updated by ECRI Institute on July 10, 2013 following the U.S. Food and Drug Administration advisory on Valproate. The currency of the guideline was reaffirmed by the developer in 2012 and this summary was updated by ECRI Institute on March 7, 2014. This summary was updated by ECRI Institute on May 24, 2016 following the U.S. Food and Drug Administration advisory on Olanzapine. This summary was updated by ECRI Institute on October 21, 2016 following the U.S. Food and Drug Administration advisory on opioid pain and cough medicines combined with benzodiazepines.

## Copyright Statement



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